Amendments to the Claims:

This listing of claims will replace all prior versions in the application:

Listing of Claims:

1. (currently amended) A method of typing a proliferative nodule ~~arising~~ in ~~association with~~ a congenital melanocytic nevus as a benign growth, the method comprising providing a nucleic acid ~~skin tumor~~ sample from the nodule ~~from a patient~~ and detecting a numerical aberration in chromosomes, wherein the numerical aberration ~~change in chromosome number in a nucleic acid sample from the skin tumor sample, wherein the change in chromosome number~~ is selected from the group consisting of a gain of whole chromosome 10, a gain of whole chromosome 11, a loss of whole chromosome 7, or a combination of these numerical aberrations, ~~thereof~~; thereby typing the nodule ~~skin tumor sample~~ as a benign growth.

2. (currently amended) The method of claim 1, wherein the numerical aberration ~~change in chromosome number~~ is a gain of chromosome 10.

3. (currently amended) The method of claim 1, wherein the numerical aberration ~~change in chromosome number~~ is a gain of chromosome 11.

4. (currently amended) The method of claim 1, wherein the numerical aberration ~~change in chromosome number~~ is a loss of chromosome 7.

5. (currently amended) The method of claim 1, further comprising detecting a gain or loss of another whole chromosome.

6. (original) The method of claim 1, wherein the detecting step comprises:

contacting a nucleic acid sample from the patient with a probe which selectively hybridizes to a target polynucleotide sequence on a chromosome selected from the group consisting of chromosome 10, chromosome 11, and chromosome 7; wherein the probe is

contacted with the sample under conditions in which the probe binds selectively with the target polynucleotide sequence to form a stable hybridization complex;

detecting the formation of the hybridization complex; and

detecting a change in chromosome number, the change selected from the group consisting of a gain of chromosome 10, a gain of chromosome 11 and a loss of chromosome 7.

7. (currently amended) The method of claim 1 6, wherein the detecting step ~~further~~ comprises an amplification reaction ~~amplifying the target nucleotide sequence~~.

8. (currently amended) The method of claim 7, wherein the ~~target nucleotide sequence is amplified using~~ amplification reaction is a polymerase chain reaction

9. (currently amended) The method of claim 6, wherein the probe ~~eprobe~~ is a centromeric probe.

10. (original) The method of claim 1, wherein the nucleic acid sample is an interphase nucleus.

11. (original) The method of claim 1, wherein the nucleic acid sample is a metaphase cell.

12. (original) The method of claim 6, wherein the probe is labeled with a fluorescent label.

13. (original) The method of claim 6, wherein the probe is labeled with digoxigenin or biotin.

14. (original) The method of claim 6, further comprising the step of blocking the hybridization capacity of repetitive sequences in the nucleic acid sample.

15. (original) The method of claim 14, wherein unlabeled blocking nucleic acids comprising repetitive sequences are contacted with the sample.

16. (original) The method of claim 15, wherein the unlabeled blocking nucleic acids are Cot-1 DNA.

17. (original) The method of claim 6, wherein the probe is bound to a solid substrate.

18. (original) The method of claim 17, wherein the probe is a member of an array.

19. (new) A method of typing a proliferative nodule in a congenital melanocytic nevus as a benign growth, the method comprising providing a sample comprising tissue from the nodule from a patient and detecting no chromosomal structural aberrations and at least one numerical aberration in chromosome, wherein the numerical aberration does not comprise a loss of whole chromosome 9 or a loss of whole chromosome 10, thereby typing the nodule as a benign growth.

20. (new) The method of claim 19, wherein the numerical aberration is a gain or a loss of a whole chromosome selected from the group consisting of 3, 4, 5, 7, 8, 9, 10, 11, 12, 15, 16, 20, 21, 22.

REMARKS

With entry of the instant amendment, claims 1-5 and 7-9 have been amended and new claims 19 and 20 have been added. Thus, claims 1-20 are currently pending.

The amendments to the claims add no new matter and are supported throughout the application as file.

Claim 1 has been amended to recite detecting a numerical aberration in chromosomes and gain of whole chromosome 10, gain of whole chromosome 11 or loss of whole chromosome 7. Support for the amendment can be found, *e.g.*, on page 4, lines 1-3 and Table 2 on page 26.

New claim 19 recites typing a proliferative nodule from a congenital melanocytic nevus as benign by detecting no structural aberrations and at least one numerical aberration in chromosomes, wherein the numerical aberrations is not a loss of chromosome 9 or 10. Support for the new claims can be found, *e.g.*, on page 23, lines 2-4 and page 21, lines 1-3.

Support for claim 20 can be found in the specification, *e.g.*, in Table 2.

The amendment to claim 9 corrects a typographical error (*see,* claim objection, paragraph 1).

For convenience, the rejections will be addressed in the order received in the Office Action mailed April 7, 2003.

The invention

The invention is a method of typing a growth in a congenital melanocytic nevus as a malignant growth (melanoma) or a non-malignant, *i.e.*, benign growth. The invention is based on the discovery that, when chromosomal abnormalities occur in atypical nodular proliferations from congenital melanocytic nevi, there are fundamental differences in the abnormalities in comparison to melanoma. These differences include the type of chromosomal aberration (those in congenital melanocytic nevi are frequently numerical, rather than structural) and the pattern of chromosomes that are involved. Such differences can be used to distinguish,

or aid in distinguishing, a benign area of growth in a congenital melanocytic nevus from melanoma.

Rejection under 35 U.S.C. § 112, first paragraph, enablement

Claims 1-18 were rejected as allegedly not enabled. Two arguments were presented. The first alleges that the claims are not enabled because they encompass detecting gains and losses in partial chromosomes as well as whole chromosomes. The second maintains that the observation of a gain of chromosome 10 or 11 in congenital melanocytic nevi in only one sample (the same sample) is inadequate to enable the invention. To the extent that the rejections apply to the amended claims, Applicants respectfully traverse.

First, the Examiner contends that the claims as filed read on detecting numerical changes in partial chromosomes. This argument is obviated by the amendments to the claims. In order to expedite prosecution, the claims have been amended to recite detection of numerical aberrations, which is defined in the specification at page 4, paragraph 17 as referring to a change in number of a whole chromosome. In addition, the claims have been amended to recite gain or loss of a whole chromosome.

Next, the Examiner argues that the claims are not enabled with regard to the gain of chromosome 10 or 11 because only one congenital melanocytic nevus that was analyzed exhibited these changes and moreover, they occurred in the same sample, which also had gains in chromosomes 16, 20, and 22. The rejection alleges that it would required undue experimentation to determine whether gain of the entire chromsome 10 or 11 alone might be associated with congenital melanocytic nevus. This argument is flawed, however, as it is not based on the totality of the data.

As noted above, the invention is a method of typing an atypical proliferating nodule in a congenital melanocytic nevus as a non-malignant growth. In the current invention, the method comprises determining the presence of numerical aberrations in the chromosomes in the congenital nevus. Loss of whole chromosome 7, gain of whole chromosome 11, and gain of whole chromosome 10 is indicative of a benign growth. The analysis provided in the examples section not only includes the congenital nevi cases, but also compares those cases to 108

melanomas. Although only one congenital melanocytic nevus sample exhibited the claimed gain of whole chromosome 10 and whole chromosome 11, these findings are in comparison to melanoma: these particular changes were observed in none of the melanoma samples (*see, e.g.*, page 21, paragraph 92 of the specification). The rejection provides no evidence or reasoning as to why the practitioner, upon observing a gain of whole chromosome 10 or whole chromosome 11 in an atypical growth from a congenital melanocytic nevus, could not reasonably expect this to be indicative of a benign growth. The such a change in at least one benign nevus sample along with its absence in any of the melanoma samples analyzed support this conclusion. Applicants therefore respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-18 were rejected as allegedly indefinite in the recitation of a number of different terms. The terms at issue are "gain of chromosome 10, a gain of chromosome 11, or a loss of chromosome 7, or a combination thereof"; typing a skin tumor sample; "a growth arising in association with a congenital melanocytic nevus"; the "detecting step" (claims 7 and 8) and "target nucleotide sequence" (claims 7 and 8).

gain or loss of chromsomes

Claim 1 has been amended to recite detection of a numerical aberration and the gain or loss of a whole chromosome. To the extent that the rejection applies to the amended claims, Applicants traverse. The claims are clear in the recitation of detecting numerical aberrations. The claimed changes are thus changes in whole chromosome number. Changes in number of partial chromosomes in the context of the invention is a structural abnormality. (paragraph 17, page 4). Applicants therefore respectfully request withdrawal of the rejection.

typing a tumor sample

Claim 1 has been amended to recite a method of typing a proliferative nodule from a congenital melanocytic nevus and to refer to the nodule in the final process step. Applicants therefore respectfully request withdrawal of the rejection.

growth arising in association with a congenital melanocytic nevus

The rejection also alleges that "a growth arising in association with a congenital melanocytic nevus" is unclear. Although Applicants disagree (the specification defines a "growth arising from a congenital nevus" as an area of proliferation in the nevus), in order to expedite prosecution claim 1 has been amended to recite a proliferative nodule from a congenital melanocytic nevus. Applicants therefore respectfully request withdrawal of the rejection.

Rejections applied to claims 7 and 8

The rejections are obviated by the amendments to the claims: claim 7 was amended to depend from claim 1, which has only one detecting step, and claims 7 and 8 were amended to omit the term target polynucleotide sequence.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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